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BIOMATERIALS

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NEW DOMESTICALLY PRODUCED IMPLANTATION MATERIALS AND THEIR APPLICATIONS IN CLINICAL PRACTICE

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Domestic and foreign implantation materials for eliminating defects and deformities in bone tissues are examined. Comparative results of experimental-morphological studies of these preparations are presented. The main results of joint scientific–applications work performed by the staff of the FGUP TsNIIAG laboratory and specialists at the jaw–face clinic at GU MONIKI are presented. A new bioceramic, calcium silico-phosphate ceramic, for replacing bone defects in jaw–face surgery, stomatology, neurosurgery, and traumatology is described.

Key words: biomaterials, biocomposites, glass ceramic, hydroxyapatite, β-tricalciumphosphate, implants, medicine.

Scientists in the leading countries in the world and in Russia doing intensive research and development work on new bioactive materials for reconstructive bone – plastic surgery. Specialists from the leading technical and medical schools in Russia are participating in this work: M. V. Lomonosov Moscow State University, D. I. Mendeleev Russian Chemical–Technology University, Tomsk Polytechnical University, Saratov State Technical University, Samara State Technical University, Samara State Medical University, and a number of other scientific centers [1 – 4].

Work on improving the chemical and mineral compositions, the macro- and microstructures of biomaterials, the study of their chemical, physicomechanical, and biological properties, which ultimately determine the success of surgical operations performed to remove bone defects, as well as the degree of functional restoration of the damaged bone tissue as an organ as a whole is being performed in these scientific centers.

Unfortunately, far from all advances by Russian scientists reach the domestic market. The yearly All-Russia Stomatological forums and DENTAL REVIEW exhibitions-fairs occurring in Moscow with the cooperation of the Russian Ministry of Health and Social Welfare are an object confirmation of this.

At these exhibits the articles made from inorganic biomaterials based on hydroxyapatite and tricalciumphosphate are represented by only a few Russian firms — Scientific and Industrial Association POLISTOM, JSC; Intermedapatit, JSC; Independent Consulting Firm "Omega Dent" — and by an entire series of foreign companies — Curasan (Germany), Geistlich (USA), Bicon (USA), Biotech (France), Scientrx (France), Synthes (Switzerland), and DS Dental (Switzerland), and others.

This situation at our home market is due to the lack of a production base for the developers of medical articles. It is difficult for the developers to complete within a rigid time frame all of the many steps of registration and certification of medical articles, predetermining the conclusion of various agreements, including mandatory medical insurance of patents and surgeons who are participating in clinic tests.

Ultimately, the results of many years of intense work by specialists in various fields are reflected in scientific publications, presentations at scientific–applications conferences, symposia, and so on, while the people who need medical help, involving, specifically, the elimination of defects in

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Fig. 1. Mechanical working of implants using a Forte-100 (Korea) brushless micromotor.

Fig. 2. Comminution and mixing of raw materials in a Pulverizette-5 planetary mill (Germany).

bone tissue, cannot obtain the benefit of the advances made by Russian scientists.

In this case doctors propose to their patients imported medical preparations. At the same time comparative morphological and clinical studies show that the home-based advances are at least as good as the imported analogues and in a number of cases surpass then with respect to quality and cost [5 – 6].

Comparative experimental-morphological studies of home and imported preparations (Table 1) performed by specialists at the Federal State Institution N. N. Priorov Central Scientific–Research Institute of Traumatology and Orthopedics (Moscow) convincingly prove that all the materials studied are biocompatible and resorbable matrices on whose surface a bone embryo forms. A callus forms and is remodeled most rapidly when KollapAn, which is produced in Russia, is implanted. In [6] it is also noted that KollapAn can be used as a matrix to immobilize and deliver to the site of an injury various pharmaceutical preparations, cellular elements, growth factors, and cytokines, which suppress pathologies and stimulate reparatory osteogenesis. The results of an investigation of experiments done on animals served as a basis for a clinical test of this preparation for the purpose of showing its effect on the stimulation of the reparative osteogenesis and prevention of infection. The difficult treatment of patients with comminuted fracture of long tubular bones, slowly healing fractures, and false articulation has shown that fracture consolidation is observed in 99.2% of the cases. The results of unsatisfactory treatment were observed in two patients, which constitute 0.8% of the total number of people participating in the experiment. For conventional treatment fractures that did not set and false articulation developed were observed in up to 10% of the cases.

TABLE 1. Synthetic Calcium Phosphate Materials and Preparations Based on Them

Preparation	Material composition	Producer/Country
KollapAn	Hydroxyapatite, collagen, antibiotic	"Intermedapatit"/Russia
Ostim	Hydroxyapatite	Osartis/Germany
chromos	β-tricalciumphosphate	Mathys Medical Ltd/Switzerland
Cerosorb	β-tricalciumphosphate	Curasan/Germany

One way out of this situation is for the firms manufacturing domestic implantation calcium phosphate materials to work together to take existing domestic scientific advances to certified medical products which are permitted to be used in clinical practice. In the opinion of the present authors, another possible road out of the present situation could be investing the financial resources of the enterprises in the development of their own production base.

This is the development path chosen by the enterprise defense-industrial complex Central Scientific–Research Institute of Automation and Hydraulics.

At the same time the Institute is conducting active work on integrating successful advances made in military technology as well as in civilian products [7]. So, the methods developed at the Institute for processing computer images have served as a basis for creating medical complexes equipped with computer systems for diagnostics of various pathologies.

In recent years, a laboratory for adopting promising technologies for civilian purposes has been created at the Institute and is successfully functioning. The scientific–research work performed in this laboratory is aimed at developing new artificial biomaterials which are suitable for eliminating birth defects and deformities of bone tissues. The laboratory is equipped with modern technological equipment which

Fig. 3. Machine for testing the mechanical properties of bioceramic glass BT1-FR5.0TN.D30 (Germany).

Fig. 4. Pulsed packing machine HAWO hd 260 MS 8 (Germany).

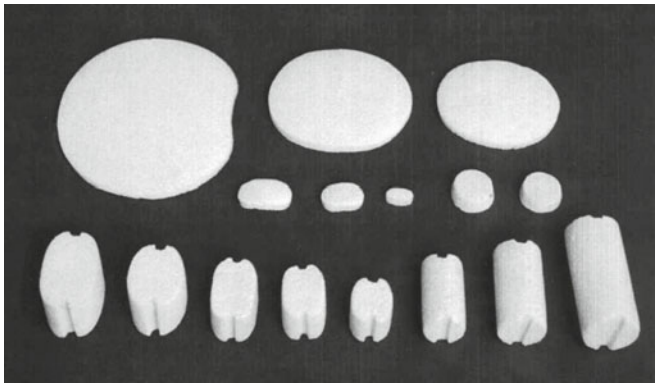

Fig. 5. Implant set NIS-NKh-R.

makes it possible to synthesize bioactive minerals, comminute and mix raw materials, perfect regimes for firing bioceramic glass, perform the necessary preclinical mechanical work, washing, drying, and packing of ready medical articles (Figs. 1 – 4).

The laboratory work performed to develop new compositions and develop technologies for obtaining composite materials continues to grow on the basis of previous results obtained in collaboration with the D. I. Mendeleev Russian Chemical Technology University and M. F. Vladimirskii GU MONIKI.

A bioactive apatitosilicate glass ceramic underwent its first medical tests at the jaw–face surgery clinic at M. F. Vladimirskii GU MONIKI. As a result of joint work performed at the end of 1990s it was proved that artificial apatitosilicate biomaterials can be used in the clinic to replace bone defects and eliminate deformities of the facial skull to 10 cm^3 in size. Methods were developed to use it in reconstructive surgery of the jaw–face region. The biocompatible composition and the porous structure of the material permit vascularization and ingrowth of the bone tissue into the implant. It was found that the apatitosilicate glass ceramic affects the healing time and healing character of bone wounds in patients as well as the restructuring time of the material depending on the size of the bone defect and the dimensions of the implant [8].

The collaboration with specialists of the neurosurgery division of the M. F. Vladimirskii GU MONIKI led to the development of a set of implants of silico-calcium phosphate neurosurgical x-ray contrast NIS-NKh-R for reconstructive operations on the roof and base of the skull and stabilization of the spine (Fig. 5). The use of the NIS-NKh-R set in clinical practice made it possible to expand substantially the available possibilities when treating patients with different bone deformities of the roof and base of the skull as well as to decrease the external immobilization time for reconstructive–stabilizing operations, traumatic injuries, and degenerative-dystrophic disease on different sections of the spine [9 – 11].

The NIS-NKh-R set has been certified and entered into the State registry of articles for medical applications and medical technology and into the register of the Federal State Unitary Enterprise “Rosoboronstandart” [12].

Work is now being done on registering and certifying silico-calcium phosphate bioceramics for replacing bone defects in the jaw–face surgery, stomatology, neurosurgery, and traumatology.

Fig. 6. Staff of the Federal State Unitary Enterprise, Central Scientific–Research Institute of Automation and Hydraulics, and the State Institution M. F. Vladimirskii Moscow Oblast Scientific–Research Clinical Institute with awards from the International Forum "High Technologies of the 21st Century" — a diploma and honorary award — the St. George gold statuette.

This material in the form of granules, blocks, and plates competes on the market with well-known home and foreign firms manufacturing similar products for use in medical treatments of the following:

– birth and acquired defects and deformities of the human bone skeleton after removal of benign bone tumors as well as traumas and inflammatory diseases;

– post-operative defects of the facial skull bones, alveolar projections of the top and bottom jaws of different etiology;

– periodontal defects of the bone tissue of the jaws.

The work performed at the Central Scientific–Research Institute of Automation and Hydraulics along these lines has been acknowledged repeatedly by awards at prestigious exhibitions. At the annual International Forum on High Technologies for the 21st Century FGUP TsNIIAG was awarded a citation and a medal (20007), diploma, and an honorary badge and at the 99th International Forum was awarded the St. George Gold Statuette (2008) (Fig. 6). At 10th anniversary specialized exhibition "Dual Purpose Articles and Technologies. Diversification the United Industrial Corporation" (2009) TsNIIG was awarded a diploma and medal for developing and manufacturing implants made with biocomposite material for eliminating defects in bone tissues.

REFERENCES

1. T. S. Petrovskaya, "Silico-phosphate glass as a component of bioactive coatings," *Steklo Keram.*, No. 12, 34 – 37 (2002); T. S. Petrovskaya, "Silicophosphate glasses as a component of bioactive coatings," *Glass Ceram.*, **59**(11 – 12), 420 – 423 (2002).
2. E. E. Stroganova, "New technologies for manufacturing and using bioceramics in restorative medicine," *Steklo Keram.*, No. 1, 37 – 38 (2008).
3. M. N. Safina, T. V. Safronova, and E. S. Lukin, "Calcium phosphate based ceramic with a resorbable phase and low sintering temperature," *Steklo Keram.*, No. 7, 19 – 24 (2007); M. N. Safina, T. V. Safronova, and E. S. Lukin, "Calcium phosphate based ceramic with a resorbable phase and low sintering temperature," *Glass Ceram.*, **64**(7 – 8), 238 – 243 (2007).
4. A. V. Belyakov, E. S. Lukin, T. V. Safronova, et al., "Porous materials based on calcium phosphates," *Steklo Keram.*, No. 10, 19 (2008); A. V. Belyakov, E. S. Lukin, T. V. Safronova, et al., "Porous materials made from calcium phosphates (Review)," *Glass Ceram.*, **65**(9 – 10), 337 – 339 (2008).
5. K. S. Desyatnichenko, N. A. Slesarenko, M. A. Kaidanovskii, and S. G. Kurdyumov, "Experimental testing of new-general osteoinducing materials by Polistom JSC," *Stomatologiya Dlya Vsekh*, No. 3, 40 – 42 (2004).
6. G. N. Berchenko, G. A. Kesyan, R. Z. Yrazgil'deev, et al., "Comparative experimental-morphological study of the effect of certain calcium phosphate materials in traumalogical-orthopedic practice on activation of reparative osteogenesis," *Byul. Vost. Sib. Nauchn. Tsentra Sib. Otd. RAMN*, No. 4, 327 – 332 (2006).
7. A. B. Shapovalov and V. V. Shcherbinin, "Dual-purpose technologies — application to medical practice," *Voennyi Parad, Spets. Vypusk*, 54 – 56 (2009).
8. M. N. Kosyakov, *Clinical-Experimental Validation of the Use of Apatitosilicate Implants for Replacing Defects and Deformities of Facial Skull Bones, Author's Abstract of Candidate's Thesis* [in Russian], Moscow (2002).
9. I. A. Kachkov, A. I. Rusinov, A. V. Kedrov, and R. G. Biktimirov, *Choice of Plastic Material and Treatment Strategy for Skull Bone Defects, Author's Abstract of Doctoral's Thesis* [in Russian], MONIKI, Moscow (2004).
10. I. A. Kachkov, A. V. Kedrov, R. G. Biktimirov, et al., *Use of BAK-1000 Implants for Frontal Stabilization of Neck Region of the Spine Subjected to Traumatic Injury, Author's Abstract of Doctoral's Thesis* [in Russian], MONIKI, Moscow (2004).
11. A. I. Rusinov, *Sculpting of Skull Defects Using Biocomposite Apatitosilicate Cellular Implant* [in Russian], Moscow (2001).
12. A. B. Shapovalov, E. B. Vlasova, A. A. Nikitin, and A. V. Kedrov, "Implant production at a defense enterprise," *Voennyi Parad, Spets. Vypusk*, 57 – 59 (2009).